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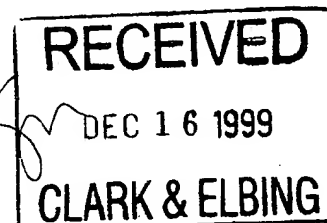
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APPLICATION NUMBER	FILING DATE	GRP ART UNIT	FIL FEE REC'D	ATTORNEY DOCKET NO.	DRWGS	TOT CL	IND CL
09/365,576	08/02/99	1646	\$1,016.00	00786/246002	20	27	3

KAREN L ELBING PH.D
CLARK & ELBING LLP
176 FEDERAL STREET
BOSTON MA 02110



Receipt is acknowledged of this nonprovisional Patent Application. It will be considered in its order and you will be notified as to the results of the examination. Be sure to provide the U.S. APPLICATION NUMBER, FILING DATE, NAME OF APPLICANT, and TITLE OF INVENTION when inquiring about this application. Fees transmitted by check or draft are subject to collection. Please verify the accuracy of the data presented on this receipt. If an error is noted on this Filing Receipt, please write to the Office of Initial Patent Examination's Customer Service Center. Please provide a copy of this Filing Receipt with the changes noted thereon. If you received a "Notice to File Missing Parts of Application" ("Missing Parts Notice") in this application, please submit any corrections to this Filing Receipt with your reply to the "Missing Parts Notice." When the PTO processes the reply to the "Missing Parts Notice," the PTO will generate another Filing Receipt incorporating the requested corrections (if appropriate).

Applicant(s) DAVID MOORE, BELLAIRE, TX; WONGI SEOL, CAMBRIDGE, MA;
HUENG-SIK CHOI, KWANGJU, REPUBLIC OF KOREA.

CONTINUING DATA AS CLAIMED BY APPLICANT-

THIS APPLN IS A DIV OF 08/372,652 01/13/95 PAT 5,932,699

IF REQUIRED, FOREIGN FILING LICENSE GRANTED 08/18/99

TITLE

RETINOID X RECEPTOR-INTERACTING POLYPEPTIDES AND RELATED MOLECULES
AND METHODS

PRELIMINARY CLASS: 530

DATA ENTRY BY: DUCKETT, GOIGA

TEAM: 08 DATE: 12/13/99

|||||

(See reverse for new important information)

Certificate of Mailing

Date of Deposit August 2, 1999

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I hereby certify under 37 C.F.R. § 1.10 that this correspondence is being deposited with the United States Postal Service as "Express Mail Post Office to Addressee" with sufficient postage on the date indicated above and is addressed to: BOX PATENT APPLICATION, Assistant Commissioner for Patents, Washington, D.C. 20231.

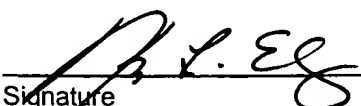
Sandra E. Marxen

Printed name of person mailing correspondence


Signature of person mailing correspondence

UTILITY PATENT APPLICATION TRANSMITTAL UNDER 37 CFR §1.53(b)

Attorney Docket Number	00786/246002
Applicant	David Moore <i>et al.</i>
Title	RETINOID X RECEPTOR-INTERACTING POLYPEPTIDES AND RELATED MOLECULES AND METHODS
PRIORITY INFORMATION:	
This application is a divisional of and claims priority from United States patent application 08/372,652, filed January 13, 1995.	
APPLICATION ELEMENTS:	
Cover sheet	1 page
Specification	43 pages
Claims	4 pages
Abstract	1 page
Drawing	20 pages
Combined Declaration and POA, which is: ■ Unsigned;	3 pages
■ A copy from prior application 08/372,652 and the entire disclosure of the prior application is considered as being part of the disclosure of this new application and is hereby incorporated by reference therein.	2 pages
Statement Deleting Inventors	
Sequence Statement	
Sequence Listing on Paper	
Sequence Listing on Diskette	
Small Entity Statement, which is: ■ Unsigned	1 page
Preliminary Amendment	

IDS	
Form PTO 1449	
Cited References	
Recordation Form Cover Sheet and Assignment	
Assignee's Statement	
English Translation	
Certified Copy of Priority Document	
Return Receipt Postcard	1
FILING FEES:	
Basic Filing Fee: \$380	\$380.00
Excess Claims Fee: 27 - 20 x \$9	\$63.00
Excess Independent Claims Fee: 3 - 3 x \$39	\$0
Multiple Dependent Claims Fee: \$130	\$0
Total Fees:	\$443.00
<input type="checkbox"/> The filing fee is not being paid at this time. <input type="checkbox"/> Please apply any other charges, or any credits, to Deposit Account No. 03-2095.	
CORRESPONDENCE ADDRESS:	
Karen L. Elbing, Ph.D. Reg. No. 35,238 Clark & Elbing LLP 176 Federal Street Boston, MA 02110	
Telephone: 617-428-0200 Facsimile: 617-428-7045	
 Signature	<u>2 August 1999</u> Date

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled RETINOID X RECEPTOR-INTERACTING POLYPEPTIDES AND RELATED MOLECULES AND METHODS the specification of which

☒ is attached hereto.

☐ was filed on _____ as Application Serial No. _____
and was amended on _____.

☐ was described and claimed in PCT International Application No. _____
filed on _____ and as amended under PCT Article 19 on _____.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose all information I know to be material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56(a).

FOREIGN PRIORITY RIGHTS: I hereby claim foreign priority benefits under Title 35, United States Code, §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed:

Country	Serial Number	Filing Date	Priority Claimed?
			Yes/No

PROVISIONAL PRIORITY RIGHTS: I hereby claim priority benefits under Title 35, United States Code, §119(e) and §120 of any United States provisional patent application(s) listed below filed by an inventor or inventors on the same subject matter as the present application and having a filing date before that of the application(s) of which priority is claimed:

Serial Number	Filing Date	Status

NON-PROVISIONAL PRIORITY RIGHTS: I hereby claim the benefit under Title 35, United States Code, §120 of any United States application(s) listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States application in the manner provided by the first paragraph of Title 35, United States Code, §112, I acknowledge the duty to disclose all information I know to be material to patentability as defined in Title 37, Code of Federal Regulations, §1.56(a) which became available between the filing date of the prior application and the national or PCT international filing date of this application:

Serial Number	Filing Date	Status
08/372,652	January 13, 1995	Pending

I hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Paul T. Clark, Reg. No. 30,162, Karen L. Elbing, Ph.D. Reg. No. 35,238, Kristina Bieker-Brady, Ph.D. Reg. No. 39,109, Susan M. Michaud, Ph.D. Reg. No. 42,885, Mary Rose Scozzafava, Ph.D., Reg. No.36,268, James D. DeCamp, Ph.D., Reg. No. 43,580.

Address all telephone calls to: Karen L. Elbing, Ph.D. at 617/428-0200.

Address all correspondence to: Karen L. Elbing, Ph.D. at Clark & Elbing LLP, 176 Federal Street, Boston, MA 02110.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Full Name (First, Middle, Last)	Residence Address (City, State, Country)	Post Office Address (Street, City, State, Country)	Citizenship
David Moore	4523 Birch Street Bellaire, TX 77401	4523 Birch Street Bellaire, TX 77401	United States
Signature:			Date:

Full Name (First, Middle, Last)	Residence Address (City, State, Country)	Post Office Address (Street, City, State, Country)	Citizenship
Wongi Seol			Republic of Korea
Signature:			Date:

Full Name (First, Middle, Last)	Residence Address (City, State, Country)	Post Office Address (Street, City, State, Country)	Citizenship
Hueng-Sik Choi	Hormone Research Center, Chonnam National University, Kwangju, 500-757 KOREA	Hormone Research Center, Chonnam National University, Kwangju, 500-757 KOREA	Republic of Korea
Signature:			Date:

COMBINED DECLARATION AND POWER OF ATTORNEY

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled RETINOID X RECEPTOR-INTERACTING POLYPEPTIDES AND RELATED MOLECULES AND METHODS, the specification of which

☒ is attached hereto.

X was filed on JANUARY 13, 1995 as Application Serial No. 08/372,652

and was amended on _____

☐ was described and claimed in PCT International Application No. _____
filed on _____ and as amended under PCT Article 19 on _____

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose all information I know to be material to patentability in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby appoint the following attorneys and/or agents to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith: Karen F. Lech, Reg. No. 35,238, William E. Booth, Reg. No. 28,933; Karl Bozicevic, Reg. No. 28,807; Barry E. Bretschneider, Reg. No. 28,055; Paul T. Clark, Reg. No. 30,162; Peter J. Devlin, Reg. No. 31,753; Willis M. Ertman, Reg. No. 18,658; David L. Feigenbaum, Reg. No. 30,378; Janis K. Fraser, Reg. No. 34,819; John W. Freeman, Reg. No. 29,066; Timothy A. French, Reg. No. 30,175; Alan H. Gordon, Reg. No. 26,168; Scott C. Harris, Reg. No. 32,030; Mark J. Hebert, Reg. No., 31,766; Gilbert H. Hennessey, Reg. No. 25,759; Charles Hieken, Reg. No. 18,411; Robert E. Hillman, Reg. No. 22,837; G. Roger Lee, Reg. No. 28,963; Steven E. Lipman, Reg. No. 30,011; Gregory A. Madera, Reg. No. 28,878; Ralph A. Mittelberger, Reg. No. 33,195; Ronald E. Myrick, Reg. No. 26,315; Robert C. Nabinger, Reg. No., 33,431; Frank P. Porcelli, Reg. No. 27,374; Eric L. Prah, Reg. No. 32,590; Alan D. Rosenthal, Reg. No. 27,833; Richard M. Sharkansky, Reg. No. 25,800; John M. Skenyon, Reg. No. 27,468; Michael O. Sutton, Reg. No. 26,675; Rene D. Tegtmeyer, Reg. No. 33,567; Hans R. Troesch, Reg. No. 36,950; John N. Williams, Reg. No. 18,948; Gary A. Walpert, Reg. No. 26,098; Dorothy P. Whelan, Reg. No., 33,814; and Charles C. Winchester, Reg. No. 21,040.

Address all telephone calls to Karen F. Lech at telephone number 617/542-5070.

Address all correspondence to Paul T. Clark, Fish & Richardson P.C., 225 Franklin Street, Boston, MA 02110-2804.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patents issued thereon.

Full Name of Inventor: DAVID MOORE

Inventor's Signature: [Signature] Date: 3/2/95

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EXTRA COPY

COMBINED DECLARATION AND POWER OF ATTORNEY CONTINUED

Full Name of Inventor: WONGI SEOL

Inventor's Signature: Wongi Seol Date: 3/27/95

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Citizen of: Republic of Korea

Post Office Address: Same

Full Name of Inventor: HUENG-SIK CHOI

Inventor's Signature: Hueng-Sik Choi Date: 4/1/95

Residence Address: Lucky HanMa Ro Apt 101-Dong, 302-Ho Yusong Gu, Taejeon

Citizen of: Republic of KOREA KOREA (SOUTH)

Post Office Address: Immunology Division, Molecular Biomedicine Group

KORZA Research Institute of Bi-science & Biotechnology

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I hereby certify under 37 CFR 1.8(a) that this correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated above and is addressed to: Assistant Commissioner of Patents, Washington, D.C. 20231.

Colleen Coyne

Printed name of person mailing correspondence

Colleen Coyne

Signature of person mailing correspondence

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: David Moore et al.

Art Unit: 1646

Serial No.: 09/365,576

Examiner: M. Pak

Filed: August 2, 1999

Customer No.: 21559

Title: RETINOID X RECEPTOR-INTERACTING POLYPEPTIDES AND RELATED MOLECULES AND METHODS

Assistant Commissioner for Patents
Washington, D.C. 20231DECLARATION OF DR. DAVID MOORE UNDER 37 C.F.R. § 1.131

I, David Moore, declare that:

1. I am an inventor of the invention described and claimed in the above-identified patent application.
2. The present claims of the application recite retinoid X receptor-interacting proteins that have an amino acid sequence that is at least 85% identical to that of RIP15.
3. The other inventors and I conceived of, and reduced to practice, the claimed subject matter of the present application prior to November 10, 1993.
4. The reduction to practice of the claimed invention is evidenced by Exhibits 1 and 2 annexed hereto. The dates of Exhibits 1 and 2 have been redacted in accordance with the standard practice, but are all prior to November 10, 1993. The experiments described and summarized in Exhibits 1 and 2 were performed by Wongi Seol, another inventor of the claimed invention. These experiments were carried out in the United States prior to November 10, 1993.

5. As described in the present application, we performed an *in vivo* interaction trap assay to isolate cDNA molecules encoding proteins that interact with the retinoid X receptor (RXR). For this assay, a mouse cDNA library was introduced into yeast that express a LexA-RXR fusion protein and that contain -galactosidase and LEU2 genes under the control of LexA binding sites. LexA-RXR is not a strong transcriptional activator in yeast. However, LexA-RXR activates expression from LexA binding sites in cells which also express a fusion protein consisting of a transcriptional activation domain joined to another protein which interacts specifically with RXR (as described on pages 12 and 25-27 of the specification).

Clone 15 which encodes RIP15 was isolated in this assay based on its ability to induce expression of both -galactosidase and LEU2, indicating that it encoded a protein that interacted with RXR.

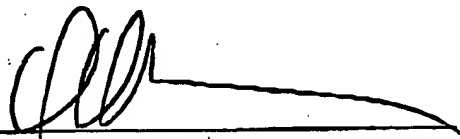
6. Exhibit 1 is a laboratory notebook page that contains a picture of an agarose gel showing the analysis of the plasmid isolated from selected yeast clone 15 and transferred into *E. coli* for analysis (lower panel). The plasmid was purified from *E. coli* and digested with restriction enzymes to determine the size of the cDNA insert in the plasmid. Based on the migration of the restriction enzyme-digested cleavage product in the agarose gel, the cDNA insert was approximately 4.0 kDa (lower left corner of Exhibit 1). A region from this cDNA insert was used as a hybridization probe to isolate the full-length RIP15 coding sequence from a mouse cDNA library, as described on page 27 of the specification.

7. This full-length RIP15 cDNA was sequenced prior to November 10, 1993. Exhibit 2 contains exemplary RIP15 cDNA sequence. In particular, the sequence of primer ip15 PCR 42merf which is listed in Exhibit 2 was designed based on the 5' terminus of this full-length RIP15 cDNA sequence. This primer was used to amplify the RIP15 sequence and add restriction sites flanking the RIP15 sequence to facilitate subsequent subcloning into an expression vector for the production of RIP15 protein. In this primer, the first nucleotide of the second RIP15 codon was altered to generate an NcoI restriction site and Kozak consensus nucleotides were included upstream of the start (AUG) codon to maximize expression of RIP15 protein. The nucleotides from the RIP15 cDNA sequence that were included in this primer are 5'-CTTCCCCCACAAGTTCTCTG-3'.

8. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are

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Date: 12/21/01

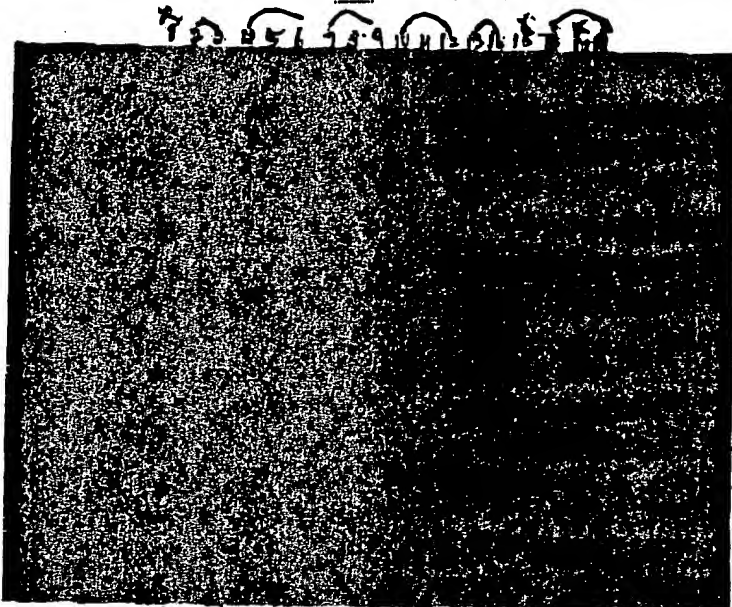

David Moore, Ph.D.
Professor
Molecular & Cellular Biology
Baylor College of Medicine

RRXR - in vivo screening

from (P)

Plasmid isolation from E. coli MC1061/P3, transformant w/ No. 2, 58
7. 101-104, 106, 108, 109. C12 plate

each 3 colonies selected for mini prep → digestion w/ HincII



BstXI
298-80

CgtII/HincII (95, 200, 2500
1.4 260, 3000
330, 4700)

2.5/1.3/0.14, 4.12, 0.15
0.25, 1.7

HincII digestion

EcoRI 2370

Pam2 2985

BstXI 2380/10

R2/PamH2

CgtII 6.65 / 0.65
vector
itself

many ... Vector p2

(15)

→ Back to yeast transformation No. 2(5) No. 4(5=6) No. 7(8=9) No. 10(11=12)
No. 13(14) No. 15 No. 16(18) No. 17 No. 19(20=21)
No. 22 No. 23(24) No. 25(26=27) No. 28(29) No. 31(32=33)
No. 34(35)
No. 1 vector No. 2 R2/PamH2 No. 5 No. 6 No. 7 No. 10

No. 3 104, 107 → just vector itself

→ forget it → no use

No. 1 0? No. 101 18(2=18) ~2.0 kb

No. 2 24=5=6 ~2.3 kb No. 102 18=20=21 ~1.4

No. 5 7=8=9 1.9 kb No. 105 18=29 ~2.3

No. 6 10=11 2.0 No. 106 31=32=33 1.0 kb

No. 7 12 1.4 No. 108 104=107 → CgtII p2?

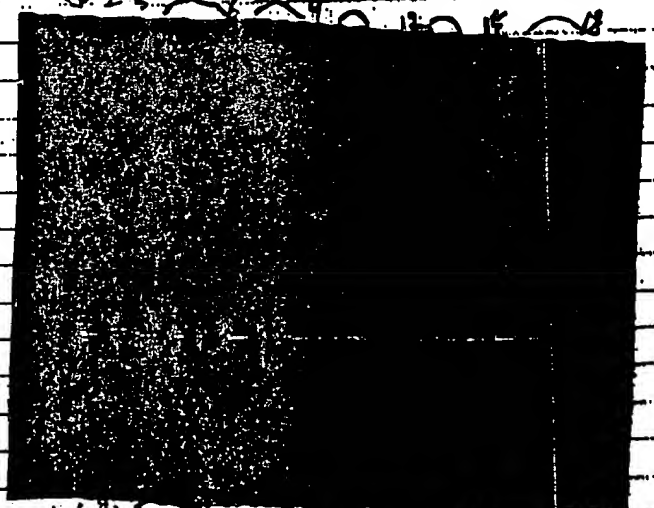
No. 13 19=14 2.0 No. 109 104=107 → CgtII p2?

No. 15 5 ~4.0

→ 943 → blue

→ 943 → blue

* 2.1 needs yeast



101 103 104 105 106 107 108 109

Brian :

Please make these oligomers. Thanks.

Wongi

p14 PCR 36mer

5'

GCG CGC AAG CTT GCC ACC ATG GCC GCG GCA TCG
Hind III Not I

GCA

p15 PCR 42mer

5'

GCG CGC AAG CTT GCC ACC ATG ~~GCT~~ TCC CCC ACA AGT
Hind IIITCT ~~CTG~~ CTG